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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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TOWNSEND AND TOWNSEND AND CREW, LLP TWO EMBARCADERO CENTER EIGHTH FLOOR SAN FRANCISCO, CA 94111-3834			GUIDRY, GUY L	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 03/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/688,299

Applicant(s)

FINN ET AL.

Examiner

Guy Guidry, Ph.D.

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) 26-39 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 40 is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 2/18/2004.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

This is a First Office Action on the Merits of the Application filed 16 October 2003. The preliminary amendments filed 1 April 2004 and 19 December 2005 have been entered. Claims 1-40 were originally filed. Claims 26-39 have been withdrawn and claim 40 amended in the December 2005 filing. In addition, Applicants further select SEQ ID No: 19 with respect to claim 8. Claims 1-25 and 40 are pending in this application.

Election/Restrictions

Acknowledgement is made of the response filed 12/19/2005, where Applicants elect to prosecute Group I (claims 1-25 and 40) with traverse. The traversal is on the grounds that there would be no undue search burden with regards to the entirety of the claimed inventions (Groups I-IV inclusive). This is deemed not persuasive. The nucleic acids of groups I-III each represent a patentably distinct product because each encodes a distinct polypeptide. A search for one of the sequences would not fully encompass the others and therefore constitute a burdensome search on the examiner. Further, search of all the inventions would encompass disparate search fields that include both the nucleic acid vectors of groups I-III and the methods of delivering or expressing a protein in a cell of IV. Product sequences and methods of protein expression in cells have a separate status in the art and because of their recognized divergent subject matter, require separate fields of search. In addition, a search amongst all the claimed sequences SEQ ID Nos: 1-46, 50 and 51 would not necessarily be coextensive with any

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other search. For example, the various sequences encompassed by the different inventions range from tens to hundreds of residues, where each distinct structure may have an inherently function differently in expression of the nucleic acid encoding the protein of interest. The sequences coding for secretion domains are from disparate sources, such as cytokine signal sequences, artificial sequences, viruses (e.g. HIV and HSV), and eukaryotic organisms and that are themselves distinct as to the particular domain's ability to transport a linked molecule into a cell (e.g. TAT or VP22). Moreover, each particular secretion domain may be involved in totally distinct mechanisms in achieving the desired outcome of cell membrane translocation when fused to an RNA polymerase (RNAP). For example, the claims are directed to 45 different structures, purportedly implying that each is interchangeable if not in structure then in function. The function for each is predicated on the interaction between the particular cellular membrane and particular protein transduction domains which is fused to a RNAP. However, at least some of the 45 different transduction domains operate by distinct and to a certain level cell-specific mechanism (e.g. HIV TAT requires cell surface heparan sulfate proteoglycans for membrane transduction while transduction domain, Antennapedia third helix, does not). In effect, a search of the non-patent literature would be vast, because each particular protein transduction domain would inherently involve distinct elements, components or steps necessary to achieve the desired outcome of membrane translocation, necessitating a separate search for each. Therefore, the requirement is still deemed proper and is made FINAL.

Claims 26-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. In addition, SEQ ID Nos: 1-7 and 9-45 are withdrawn as directed to non-elected species.

Specification

The specification is objected to for the following informalities.

The proper use of the trademark has been noted in the specification, on page 39 for example. Similar trademark designations are missing for TritonTM X-100 on page 53, lines 4 and 16, and for RiboQuantTM RPA on page 54, line 10.

The brief description of the drawings is objected to for incorrect labels. The labeling of figure 9 is not consistent with the brief description because the case of the letter designations is not consistent between description and drawing. Specifically, the description recites Fig 9A (pg. 12 line 5) and Fig 9B (pg. 12, line 14) whereas drawing for figure 9 shows two parts labeled a) and b). Appropriate correction is required

Claim Objections

Claims 19, 23 and 24 are objected to for the following informalities. Claims 19, 23 and 24 contain an acronym without corresponding definition. The objection could be overcome by the incorporation of a definition in claim 14, which currently recites a "polyethyleneglycol-lipid"

Claim Rejections - 35 USC § 101

35 U.S.C. §101 states:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 11 is rejected under 35 USC §101 because the claimed invention is directed to non-statutory subject matter. The specification contemplates *in vivo* gene therapy which encompasses gene therapy in humans. For example, section VIII Methods of Treating Disease on p. 42 of the specification (see especially the entire section) embraces embodiments of the claimed inventions that include methods for treating cancers, autoimmune diseases, cardiovascular diseases, cystic fibrosis, sickle cell anemia, hemophilia, viral, bacterial and inflammatory diseases. Also, methods for treating disease are recited on page 34, lines 10-11 (treatment of cancers), p. 35, lines 13-15 (angiogenesis and cancer treatment) and pp. 35-36 (cytotoxic/suicide genes for gene therapy). The term "host cell" recited in claim 11 is not explicitly defined in the specification. Therefore, the cell may be present or intended to be present in a human being, said cell becoming integrated into the human being and therefore being an inseparable part of the human itself. The scope of the claim, therefore, encompasses a human being, which is non-statutory subject matter. As such, the recitation of the limitation "isolated host cell" would be remedial. See 1077 O.G. 24, April 21, 1987.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25 are rejected under 35 USC 112, 1st paragraph, as failing to comply with the written description requirement.

The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the claims are directed to any secretion domain that is fused to a RNA polymerase(s) (RNAPs) which must have the prescribed function of facilitating membrane translocation while concomitantly not hindering RNAP function. Thus, the claims are directed to a genus in terms of a fusion structure containing a domain allowing for membrane translocation while preserving RNAP function.

Given the number of potential secretion domains that can be fused with various RNAPs, the number of potential RNAP-secretion domain fusion protein combinations would be large. The written description requirement for a claimed genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, disclosure relevant identifying characteristics coupled with a known or disclosed correlation between function and

structure or some combination sufficient to show applicant was in possession of the claimed genus.

The specification discusses secretion domains (signal peptides and protein transduction domains, specification pp. 23-24) polypeptide sequences which when linked to another polypeptide are given to create fusion proteins that are able to enter cells upon cell contact. However, the only relevant examples of secretion domain-RNAP fusion proteins are limited to two specific embodiments of which are SEQ ID NOs: 1 and 21, fused to a T7 RNA polymerase and used to transfect Neuro 2A cells and BHK cells respectively (specification pp. 50-54 1, Examples 2-3). SEQ ID NO: 1 is directed to a HIV TAT domain, which would be limited to particular cell types, because HIV TAT requires cell surface heparan sulfate proteoglycans to facilitate membrane transduction (see especially the Abstract of Rusnati et al., 1997, J. Biol. Chem., 272(17): 11313-11320 and the Abstract and pages 3256-7 of Tyagi et al., 2001, J. Biol. Chem., 276(5):3254-61). Therefore in determining the identity of various fusion constructs that would encode secretion competent RNAPs, one of skill would have to be apprised of the particular mechanisms by which the secretion domains facilitate membrane transduction.

Structural comparisons between known protein transduction domains (PTDs) provide little insight, however, into the mechanism of transduction. (e.g. Schwarze and Dowdy. Trends Pharmacol. Sci., 2000, 21:45-8; p. 45, col. 3). Given that the various secretion domains vary in size from tens to hundreds of amino acids, one could not envisage which structures would encode secretion domain-RNAP fusion proteins where

the size of the secretion domain would not confer steric interference of polymerase activity. Moreover, in referring to secretion domains, it is important to note that not all proteins are the same and, therefore, one (membrane transduction) protocol will not work for all proteins (see Schwarze et al., *supra*, p. 46; discussing different protein transduction domains, including TAT and VP22). In sum, the disclosure is not descriptive of the complete structure of a representative number of species, which the claims encompass, as one of ordinary skill in the art cannot envision all structures based on the teachings in the specification. With respect to the particular secretion domain disclosed (i.e. claim 8, SEQ ID NO:19 encoding an IL-2 secretion domain), one of skill would not be able to envisage the broad genus of any RNAP, with which the IL-2 secretion domain fusion would function in both translocation across any cellular membrane while preserving polymerase activity.

Given the large breadth of the fusion secretion domain-RNAPS embraced by the rejected claims, and given the limited description from the instant specification of such fusion proteins, the skilled artisan would not have been able to envision a sufficient number of specific embodiments to describe the broadly claimed genus of secretion domain-RNAP fusion proteins. Moreover, an applicant claiming a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from other species. Therefore, the skilled artisan would reasonably have concluded that Applicants were not in possession of the claimed invention.

Claims 1-25 are rejected under 35 U.S.C. 112, 1st paragraph, as failing to comply with the enablement requirement.

The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. While enabling for a methods for creation of two fusion RNA polymerases (RNAP), specifically VP22-T7-RNAP and TAT-T7-RNAP, the specification does not enable a person of skill in the art to which it pertains to make and use the broad genus of any secretion domain-RNAP commensurate in scope with the claims. In addition, the claims read on gene therapy, insofar as being directed to a vector containing a secretion domain-RNAP fusion protein in a vector to encode a therapeutic product of interest. By definition the term "therapeutic" reads on *in vivo* application and in the context of the instant invention such an *in vivo* application would necessarily be defined as gene therapy. Therefore, the only disclosed utility for the given claimed composition is gene therapy.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916). See also *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) and *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

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- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Breadth of the claims/ nature of the invention

The claims are broad in scope in that base claim 1 is directed to vast combination of secretion domain-RNAP fusion proteins, as discussed above. Specifically, the claims are directed to a genus of secretion domains that is fused to a genus of RNA polymerases (RNAPs) which must have the prescribed function of facilitating membrane translocation while concomitantly not hindering RNAP function. Thus, the claims are directed to a genus in terms of a fusion structure containing a domain allowing for membrane translocation while preserving RNAP function; consequently, the number of potential RNAP-secretion domain fusion protein combinations would be substantial. Structural comparisons between known protein secretion domains are not always informative with respect the mechanism of transduction (see Schwarze et al., *supra*, Trends Pharmacol. Sci., 2000, 21:45-8; p. 45, col. 3). Given that the various secretion domains vary both in size and presumptive method of membrane translocation, the specification is not enabling for construction of a genus of structures which would encode secretion domain-RNAP fusion proteins where the size of the secretion domain would not confer steric or functional interference of polymerase activity. Therefore, the disclosure is not enabling for a genus of structures

(secretion domain-RNAPs) which the claims encompass. In addition, the claims are broad in being directed to membrane transduction (i.e. cell transfection) of any cell in any organism. As noted previously, the invention is directed to expression of therapeutic products in claims 9 and 10, which necessarily reads on *in vivo* application and in the context of the instant claims would read on gene therapy.

State of the art/unpredictability of the art

As indicated above, one of skill would not be able to envisage all the structures encompassed by the claims, given the prescribed functionality, thus there would be a large degree of unpredictability in regard to the various secretion domain-RNAP fusion proteins. Specifically, it would be unpredictable whether the secretion domain-RNAP fusion would both traverse any cell membrane and subsequently whether the RNAP would function in catalyzing transcription. Therefore, in determining the identity of various fusion constructs that would encode secretion competent RNAPs, one of skill would have to be apprised of the particular mechanisms by which the secretion domains facilitate membrane transduction. For example, HIV TAT domain would not form a secretable RNAP for a genus of membranes because TAT requires cell surface heparan sulfate proteoglycans to facilitate membrane transduction (see especially the Abstract of Rusnati et al., 1997, J. Biol. Chem., 272(17): 11313-11320 and the Abstract and pages 3256-7 of Tyagi et al., 2001, J. Biol. Chem., 276(5):3254-61). Therefore in determining the identity of various fusion constructs that would encode secretion competent RNAPs, one of skill would have to be apprised of the particular mechanisms

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by which the secretion domains facilitate membrane transduction. As previously noted, with respect to the particular secretion domain disclosed (i.e. claim 8, SEQ ID NO:19 encoding an IL-2 secretion domain), one of skill would not be able to envisage the broad genus of any RNAP, with which the IL-2 secretion domain fusion would function in both translocation across any cellular membrane while preserving polymerase activity.

Additionally, while the level of skill of an ordinary person in the art is high, with respect to claims 9 and 10 and gene therapy, the art is highly unpredictable. For example, vectors used to deliver constructs encoding therapeutic products may be erroneously inserted into a particular gene resulting in unknown, adverse or detrimental effects (see especially Juengst, 2003, BMJ, 326: 1410-1411, discussing that gene transfer often has multiple unpredictable effects on cells). Additional obstacles to successful practice of the invention include poor efficiency of delivery of the gene to the targeted cells, poor transformation efficiency of target cells, and unpredictable and transient expression of the transgene in target cells (see especially Verma et al., Nature, 1997, 389: 239-242). Furthermore, the fusion proteins could elicit immune toxicity in the subject being treated. Assuming successful transcription, a gene of interest encoding a therapeutic product would not necessarily be translated at all, since the transcription is cytoplasmic and the mRNA not capped, the product could be degraded or be too unstable to undergo translation.

Amount of direction or guidance

There is general guidance provided to a number of types of RNA polymerases, spanning a genus that includes both phagemid/viral RNAPs to eukaryotic RNAP that could potentially function as RNAP fusions. A broad variety of membrane secretion domains, signal peptides and protein transduction domains that could presumably be employed to generate a secretable RNAP are discussed in general terms. The only specific guidance is limited to two T7-RNAPs discussed above. Also, there is general guidance provided as to the identity of some therapeutic products of interests (specification pp. 33-36) with respect to gene therapy. However, the only relevant guidance as to gene therapy or treatment of disease is prophetic in nature (e.g. single chain insulin on pp. 34-38 and suicide gene/prodrug systems pp 35-36 of the specification). Otherwise, there is no substantial relevant guidance provided as to using the claimed invention *in vivo*.

Number of working examples/level of skill/ quantity of experimentation necessary to make or use the invention.

As noted above, two working examples of secretion domain-RNAP are provided although no working example of the RNAP fusion protein recited specifically in claim 8, an expression vector with an IL-2 secretion domain-RNAP fusion construct, is noted in the specification. With respect to *in vivo* embodiments of the inventions directed in claims 9-10 and gene therapy, two examples of transfection are provided but are limited to an *in vitro* context; no relevant *in vivo* examples provided. Also, the level of skill in the art required to practice the claimed invention is high. However, given the unsolved

hurdles to successful practicing of the invention, the level of unpredictability in the art and lack of relevant working examples, it must be considered that the skilled artisan would be required to conduct experimentation of an undue nature in order to attempt to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5 and 6 are rejected under 35 U.S.C. 112 2nd paragraph for indefinite language. Claim 5 is directed to a vector where the first and second IRES are "the same" and claim 6 where they "are different". The identifiers, "same" and "different" for IRES sequences are not disclosed in the specification. As such, it is not possible to identify the boundaries of the claims because the meanings of the terms "same" and "different" are ambiguous.

Specifically, regarding claim 5, the phrase elements not actually disclosed (those encompassed by "the same"), thereby rendering the scope of the claim(s) unascertainable. Regarding claim 6, the phrase "different" renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by "different"), thereby rendering the scope of the claim(s) unascertainable. See MPEP § 2173.05(d). "the same" renders the claim(s) indefinite because the claim(s) include(s)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7, 9-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dalby et al. (US Pat. 6,773,920) in view of Deng and Wolff (Gene, 1994, 143: 245-249) as evidenced by Mizuguchi et al., (Mol Ther. 2000 Apr;1(4):376-82). Dalby et al. teach compositions where a cell-modifying polypeptide linked to a secretion domain such as T7 RNAP-VP22 may direct T7 promoted gene expression a the nucleic acid composition comprising a T7 promoter and a sequence encoding a product of interest (col. 9, lines 47-53). Dalby et al. also teach such a vector construct with a nuclear promoter (see the P_{CMV} in figs. 5 and 6). While Dalby et al. teach a method for modulating expression of a target gene by contacting a cell with a regulatory agent-translocating peptide fusion wherein the regulatory agent modulates expression of a target gene. (Col. 44, claim 5), Dalby et al. do not specifically teach a T7 polymerase autogene or the use of internal ribosome entry sites (IRES).

Deng et al. teach an autogene vector containing a T7 promoter, encephalomyocarditis (EMC) internal ribosome entry sequence (IRES), and T7 RNA polymerase and transfection and self-amplification in 3T3 fibroblasts (see especially the Introduction, p. 245, col. 2 to p. 246).

Mizuguchi et al., teach a vector with nuclear promoter and first gene upstream of an IRES-dependent second gene in a bicistronic expression vector (see especially p. 378, fig 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made, in creating an expression vector for a secreteable RNA polymerase, to design the vector so that to high levels of heterologous protein would be expressed. Therefore, a person of skill would choose a design in which high levels of transcripts possible via an autogene configuration in the manner of Deng et al. and enhanced translation in the absence of mRNA capping through the use of IRESs as taught by Deng et al. and Mizguchi et al, particularly if the vector could be generated by splicing the relatively small coding sequence for a T7 RNAP and IRES in the manner of Deng et al. and Mizguchi et al., into a preexisting vector of the type described by Dalby et al.

Absent evidence to the contrary, one would have a reasonable expectation of success in combining these teachings, a vector with a eukaryotic promoter, self amplifying secretebale polymerase and IRES sequences to facilitate translation of uncapped cytosolic message for heterologous proteins as embraced by the inventions of the instant application.

Conclusion

Claims 1-25 are rejected

Claim 40 is allowed. While secretion competent RNA polymerases are known in the prior art (see Dalby et al, *supra*, for a discussion of a VP22-T7-RNAP fusion protein) and polynucleotide sequences coding for various parts of the vector comprising SEQ ID NO: 51 are well known, including the cytomegalovirus virus (CMV) promoter, see

especially Mandel et al. (1997) PNAS 94:14083-14088, Interleukin-2 (IL-2), see especially Taniguchi et al. US Patent ,4,738,927 A, and T7 RNA polymerase, Dalby et al. as noted above, the prior art does not teach the specific nucleic acid sequence of SEQ ID NO: 51 insofar as a linear sequence comprising a CMV promoter, an IL-2 signal sequence and a sequence coding for the first 11 amino acids of IL-2 fused to a sequence coding for a T7 RNA polymerase.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Guy Guidry, Ph.D. whose telephone number is 571-272-7928. The examiner can normally be reached on Monday through Friday 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Guy Guidry, Ph.D.
Examiner
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DANIEL M. SULLIVAN
PATENT EXAMINER